REMARKS

I. Specification

An abstract of the disclosure, as required by 37 C.F.R. §1.72(b), is provided herewith on a separate sheet and made a part hereof.

II. Claim Amendments

The claims have been amended to clarify that the claimed invention is directed to a *delayed release* oral pharmaceutical dosage form, a process for making the same and methods of treatment comprising the administration of the claimed *delayed release* oral pharmaceutical dosage forms.

The claimed *delayed release* oral pharmaceutical dosage form is characterized by a core material coated with a disruptable semipermeable membrane. The claimed dosage form is not enteric coated. The core material includes the active ingredient, one or more alkaline additives and one or more swelling agents.

In the pharmaceutical industry, the expression "delayed release" is used to describe dosage forms that release discrete amount(s) of the drug some time after administration and that exhibit a lag time during which little or no absorption occurs. Support for the amendment clarifying the *delayed release* profile of the claimed dosage form is provided by the specification at page 4, lines 11-22:

> ...The core material also comprises a swelling agent that upon contact with moisture starts to swell. When the coated pellets pass the stomach small amounts of gastric fluid will be absorbed through the semipermeable membrane...At the same time the swelling agent, will be exposed to the penetrating fluid or moisture, and it will start to expand. After a predetermined time

> interval this expansion leads to disruption of the superimposed semipermeable membrane by the built-up pressure or to a swelling that will increase the permeability of the membrane. The time interval is to be determined so that the pellets have had time to pass the stomach at that very moment, and have reached the small intestines. The entire dose of the active ingredient will then start to be released into the small intestine where absorption can occur. (Emphasis added)

Thus, based on the preceding disclosure from the specification, the claimed dosage form is formulated to have a *delayed release* until such time that the dosage form has passed through the stomach and reached the small intestines. Applicants submit that the *delayed release* profile of the claimed invention is also supported by the data of Example 4. As demonstrated by Example 4 of the application, the onset or start of dissolution after two hours of pre-exposure in acid medium is delayed, and almost 3 hours are required to obtain a release of at least 73% of the active ingredient from dosage forms prepared in accordance with the claimed invention:

TIME (hours) (after 2 hours of pre-exposure in acid medium)	% release of active ingredient
0.5	3
1	18
2	60
3	73

Accordingly, Applicants submit that the specification clearly shows that the claimed invention is characterized by a *delayed release* profile. As such, the claim amendment is fully supported by the specification and, therefore, does not introduce new matter.

III. Claim Rejection – 35 U.S.C. §103(a)

Claims 1, 3-20 and 23-27 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Makino et al. (EP 0237 200) ("Makino") in view of Okada et al. (JP402237918) or US 5,776,489 to Preston et al.

For the reasons of record, the Examiner alleges that Makino contemplates both sustained-release and enteric-coated oral formulations of a benzimidazole compound. The Examiner states that Makino does not disclose a polymeric material containing a modifying agent for coating pharmaceutical dosage forms. For this reason, the Examiner relies on the secondary references for their alleged disclosure of coating films containing modifying agents, e.g., talc and fumed silica. The Examiner concludes, therefore, that it would have been obvious at the time the claimed invention was made to combine Makino with either of the secondary references to arrive at the claimed invention. Applicants respectfully submit that the cited combination of references does not suggest the claimed *delayed release* oral pharmaceutical dosage form.

Rather, Makino is limited to dosage forms having enteric or sustained release properties. For the reasons set forth in Section II, above, the claimed invention has neither enteric nor sustained release properties. Firstly, the dosage form is not enteric coated. Secondly, Makino discloses a formulation having a sustained release, i.e., formulated in such a manner as to make the contained medicament available over an extended period following ingestion. Other expressions to describe a sustained release dosage form include "prolonged-action" and "extended-release". By definition, delayed release products are not sustained release. (See http://www.australianprescriber.com/magazines/vol22no4/oral.htm) Applicants submit, therefore, that the sustained or extended release profile of Makino does not suggest the *delayed release* profile of the claimed invention wherein the dosage form must be formulated to delay

release of the medication until the dosage form, e.g., a tablet, has passed through the stomach.

Makino neither requires nor suggests a delayed release. Instead, it is sufficient for Makino's purposes that the release of the drug starts and continues any time after administration without any regard for the targeted delivery and onset of release. At the time the claimed invention was made, it was the art-recognized practice to apply an enteric coating layer to oral dosage forms of omeprazole to protect the acid-labile substance omeprazole from degradation and transformation in acidic to neutral media. Accordingly, it was unexpected that an oral formulation of omeprazole could be prepared with a disruptable semipermeable membrane, but without an enteric coating, to provide for the delayed release of the active ingredient in the small intestine where absorption can occur.

For all of the foregoing reasons, Applicants submit that the cited prior art, whether taken alone or in combination, does not suggest the claimed invention. Withdrawal of the §103 rejection is requested.

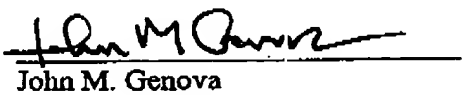
CONCLUSION

Applicants have made a good faith attempt to respond to the Office Action. It is respectfully submitted that claims 1, 3-20 and 23-27 are in condition for allowance, which action is earnestly solicited.

Any fees due in connection with this response should be charged to Deposit Account No. 23-1703.

Dated: 19 June 2003

Respectfully submitted,



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ABSTRACT

The present invention is directed to a delayed release oral pharmaceutical dosage form comprising a core material coated with a semipermeable membrane. The core material comprises an active ingredient selected from the group consisting of omeprazole, an alkaline salt thereof, *S*-omeprazole and an alkaline salt thereof, one or more alkaline additives, one or more swelling agents, and optionally pharmaceutically acceptable excipients. The dosage form is not enteric coated.